Guidance for Industry

Recommendations for Donor Questioning Regarding Possible Exposure to Malaria

DRAFT GUIDANCE

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For questions on the content of this draft guidance contact Mark Heintzelman, Ph.D., by telephone at (301) 827-3524, or by telefax at (301) 827-3534.

U.S. Department of Health and Human Services
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GUIDANCE FOR INDUSTRY[1]

Recommendations for Donor Questioning Regarding Possible Exposure to Malaria

I. INTRODUCTION

This guidance document provides the recommendations of the Food and Drug Administration (FDA) for donor questioning regarding travel to vacation resorts located in malarious regions. These recommendations apply only to donations containing intact red blood cells or platelets. Donations used for preparing plasma, plasma components or derivatives devoid of intact red blood cells or platelets are excluded. In addition, the term "resident" is being defined for the purposes of malarial deferral, to be a person that has resided in a malarious area for five years or longer. This guidance document, when finalized, will replace the recommendations in the guidance entitled, "Recommendations for Deferral of Donors for Malaria Risk" dated July 26, 1994, for deferral of blood donors for malaria risk.

II. BACKGROUND

Surveillance studies conducted by the Centers for Disease Control and Prevention (CDC) since 1974 indicated no change in the frequency of transfusion-transmitted malaria, estimated at 0.25 cases per million blood units collected, compared with the experience under previous donor deferral practices (Ref. 1). Nevertheless, more recently obtained scientific data led some researchers and the American Association of Blood Banks to reexamine the standards then in place (Ref. 2, 3) and to propose revised standards for donors at risk for malaria.

FDA brought this issue to public discussion at the June 29, 1993, meeting of its Blood Products Advisory Committee. Subsequently, FDA issued guidance to blood establishments regarding the deferral of blood donors at increased risk for malaria in a guidance of July 26, 1994, entitled, "Recommendations for Deferral of Donors for Malaria Risk." That guidance states that permanent residents of countries where malaria is not endemic and who travel to an area considered endemic for malaria by the Malaria Branch, CDC, Department of Health and Human Services, should not be accepted as donors of Whole Blood and blood components for one year after departure from the endemic area, regardless of whether or not they have received anti-malarial chemoprophylaxis. Currently, there are no approved tests to screen donated blood for malaria, careful questioning is essential for identifying prospective donors at risk for

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[1] This guidance document represents FDA's current thinking on malarial risks for prospective blood donors. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

transmitting malaria. Blood establishment personnel should carefully elicit the necessary information regarding travel and disease history in order to defer those at risk. Two recently reported fatal cases of transfusion-acquired malaria underscore the need to maintain vigilance in deferral of at-risk donor's (Ref. 4, 7).

Four species of *plasmodia* infect humans: *P. falciparum*, *P. malariae*, *P. ovale*, and *P. vivax*. They are transmitted by infected female *Anopheles* mosquitoes. The malarial organisms have a worldwide distribution and are endemic in areas with *Anopheles* mosquitoes and a human reservoir (Ref. 5). At the present time, malaria has essentially been eradicated from most of Europe, the United States, Australia, and Japan. It has not been naturally transmitted in climates such as exist in Canada, the Nordic countries, and northern Russia. The risk of developing malaria is directly proportional to the density of the human reservoir, the density of the vector population, and the resulting amount of exposure. In general, even in endemic countries, there is little risk at altitudes above 5000 feet of elevation, and less in more temperate climates. Urban areas are generally safer than rural ones (Ref. 5). Since female *Anopheles* mosquito activity occurs primarily from dusk to dawn, risk of exposure to malaria is highest at this time period. Nonetheless, it is impossible to fully identify each and every individual's exposure in an endemic area and the safety level required for the nation's blood supply necessitates that visitors to areas endemic for malaria be deferred regardless of the time of day of exposure. The Blood Products Advisory Committee discussed this issue at their June 1999 meeting, and voted against allowing travelers to endemic areas to donate blood, regardless of the time of day for the travel.

FDA has received requests for clarification regarding whether exclusion of travelers as blood donors, should include visitors to resorts *located in rural areas in Mexican states considered at risk for malaria by the CDC* (as listed in CDC's *Health Information for International Travelers,* known as the "CDC Yellow Book" or on CDC's web site, www.CDC.gov). This issue was discussed at a public meeting of FDA's Blood Products Advisory Committee on December 12, 1996. Since that time, FDA has reviewed the available information on risk of malaria at Mexican resorts. CDC provides information regarding these geographical areas and the risk of malaria.

Blood establishments are advised that the "CDC Yellow Book" is revised periodically by the CDC, and blood establishment Standard Operating Procedures and deferral practices should keep pace with such revisions. The level of safety required for the blood supply necessitates that standards be set such that risks for malaria that may not require chemoprophylaxis for travelers may result in deferral as a blood donor.

III. RECOMMENDATIONS

FDA's recommendations for deferral of blood donors at increased risk for malaria are as follows:

1. Permanent residents of non-endemic countries who travel to an area considered endemic for malaria by the Malaria Epidemiology Section, CDC, should not be accepted as donors of Whole Blood and blood components, including platelets, prior to one year after departure from the endemic area. After one year has passed since departure from the malarious area, such otherwise suitable prospective donors may be accepted provided that they have been free of unexplained symptoms suggestive of malaria and regardless of whether or not they have received antimalarial chemoprophylaxis.

2. Prospective donors who have had malaria and received an appropriate treatment should be deferred for three years after becoming asymptomatic.

3. Persons that have previously resided in endemic countries and now reside in the United States, such as immigrants, refugees, citizens, or residents (for at least five years) of endemic countries should not be accepted as donors of Whole Blood or blood components, including platelets, prior to three years after departure from the area. After the three year period, otherwise suitable prospective donors may be accepted if they have remained free of unexplained symptoms suggestive of malaria.

4. Persons that may possess a partial acquired immunity to malaria, such as those that have previously resided in a malarious region for at least five years (immigrants, refugees, citizens, persons who have been or who are residents of endemic countries), should not be accepted as donors of Whole Blood or blood components, including platelets, for a period of three years since their last *visit* to a malarious region.

5. The following questions should be added to the donor questionnaire:

a) *"Were you born in the United States?"*

If the answer is **yes**, the donor should be asked,

b) "Have you traveled outside of the United States in the last three years?"

If so, determine if the area visited was a malarious area that should result in donor deferral.

If the answer to the question "*Were you born in the United States*" is **no**, the donor should be asked,

i) *"When did you arrive in the United States?"* and

ii) *"Since your arrival, have you traveled outside the United States?"*

If the answer to the question in "5a" (above) is **yes**, or if in question "ii" (above) it is determined that the prospective donor has traveled out of the United States, follow-up questions should be asked to determine the country or geographical regions that have been visited.

Blood collection facilities should further question the prospective donor regarding exposure history to better ascertain the actual risk of exposure to malaria using the information contained in the BACKGROUND section of this document. If questions persist about whether a prospective donor traveled to a malaria endemic area, call the Malaria Epidemiology Section, CDC, at (770) 488-7788. For other questions concerning malarial risk and donor suitability, please contact the Division of Emerging and Transfusion Transmitted Diseases, Center for Biologics Evaluation and Research, FDA at (301) 827-3011.

When more than one deferral period applies to a donor, the longest period of deferral should go into effect.

IV. IMPLEMENTATION

The recommendations contained in this guidance may be implemented immediately without prior approval from the FDA. Under 21 CFR 601.12 licensed establishments implementing these recommendations should submit by official correspondence a statement in their annual report indicating the date that the revised standard operating procedures, consistent with these recommendations, have been established and implemented.

Questions concerning these recommendations should be directed to the Division of Blood Applications, Office of Blood Research and Review, Center for Biologics Evaluation and Research, FDA at (301) 827-3524, FAX (301) 827-3534.

V. REFERENCES

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